The People's Trial Materials
May 19, 2022

ATTACHMENT 1

Designation Run Report

Narayana, Arvind (PLAYED IN SF 5.19.2022)

Narayana, Arvind 09-30-2021

Plaintiff Affirmatives 00:16:14

Defense Counters 00:01:01

Plaintiff Response Designations 00:00:16

Total Time 00:17:31

NA02-Narayana, Arvind (PLAYED IN SF 5.19.2022)

Page/Line	Source	ID
43:20 - 43:22	**Narayana, Arvind 09-30-2021 (00:00:08)** 43:20 Q. Who is -- tell me who is, let's see, 43:21 Dayno, Jeffrey Dayno? Wasn't he your supervisor? 43:22 A. Yep.	NA02.1
50:02 - 50:18	**Narayana, Arvind 09-30-2021 (00:00:47)** 50:2 It says, "Arvind, can you please help me 50:3 understand more about your plans with regard to 50:4 Item 4?" 50:5 And it says, "Item 4, when did we agree 50:6 to discuss the specifics of deaths in public?" 50:7 MR. PAPANTONIO: Stop right there. Underline 50:8 that for me. I can't -- before we move on, there 50:9 is a lot packed into this paragraph. Underline 50:10 that for me, would you. 50:11 BY MR. PAPANTONIO: 50:12 Q. "When did we agree to discuss the 50:13 specifics of deaths in the public?" 50:14 Now, with that line up there, Doctor, 50:15 why don't you tell the jury how a person goes about 50:16 dying from a drug overdose. Tell me the physiology 50:17 of how a person stops breathing from a drug 50:18 overdose.	NA02.2
50:21 - 51:08	**Narayana, Arvind 09-30-2021 (00:00:42)** 50:21 Q. Do you know enough to be able to tell me 50:22 that? 50:23 A. I mean, when -- when an opioid is given 50:24 at a high enough dose or if it's given frequently 51:1 enough, the patient will have I think a reduction 51:2 in their ability to breathe to the point in some 51:3 cases where they can stop breathing, which -- 51:4 which you -- unless -- unless -- unless they're 51:5 given something like Naloxone, they would probably 51:6 die. 51:7 So, yeah. So, it's a known -- a known 51:8 serious side effect of opioids, including ours.	NA02.3
52:15 - 52:19	**Narayana, Arvind 09-30-2021 (00:00:11)** 52:15 Q. this is 52:16 Penny that's writing this, correct? Penny is 52:17 writing this. Why don't you tell the jury a little 52:18 bit more about Penny so we can understand these	NA02.4

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	52:19 words as we go forward. Tell us about Penny.	
52:22 - 53:06	**Narayana, Arvind 09-30-2021 (00:00:21)**	NA02.5
	52:22 A. Penny was the regulatory lead for 52:23 Fentora by my understanding. So, she was -- she 52:24 reported I believe to Eric Floyd. 53:1 BY MR. PAPANTONIO: 53:2 Q. And regulatory lead is they're the ones 53:3 talking to the FDA and supposed to be giving them 53:4 all the information, good and bad, about their 53:5 product, right? 53:6 A. Yes.	
55:07 - 55:23	**Narayana, Arvind 09-30-2021 (00:00:55)**	NA02.6
	55:7 Your company was 55:8 trying to expand the use of Fentora to things like 55:9 back pain and migraine headaches. And I'm not even 55:10 sure you knew that, did you? 55:11 A. Oh, I mean, I was involved in all the 55:12 discussions. I didn't make the final decisions in 55:13 some cases. But I will note that, yes, low back 55:14 pain was -- so, low back pain in opioid-tolerant 55:15 patients. 55:16 Migraines, I don't think that we ever 55:17 considered migraines as part of an indication that 55:18 we were seeking unless those patients were 55:19 opioid-tolerant. 55:20 So -- so, I think that migraines is 55:21 something we never really talked about. Low back 55:22 pain and chronic neuropathic pain we did. That was 55:23 the goal of the supplementary application.	
63:16 - 63:19	**Narayana, Arvind 09-30-2021 (00:00:12)**	NA02.7
	63:16 Q. We already know that you told us 63:17 that when Juergen went to the FDA, they did not 63:18 approve the use of your product, Fentora, for 63:19 anything except cancer pain, correct?	
63:23 - 63:23	**Narayana, Arvind 09-30-2021 (00:00:01)**	NA02.8
	63:23 A. Yes, that's correct.	
265:14 - 265:21	**Narayana, Arvind 09-30-2021 (00:00:18)**	NA02.9
	265:14 Doctor, this document is entitled 265:15 "Fentanyl Buccal Tablet, Review and Assessment of 265:16 Risks for Abuse and Diversion."	

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	265:17 Do you see that?	
	265:18 A. Yes.	
	265:19 Q. Have you seen this document before?	
	265:20 A. I think so. But, yeah, can't recall	
	265:21 for -- yeah.	
266:20 - 267:01	**Narayana, Arvind 09-30-2021 (00:00:17)**	NA02.10
	266:20 Q. Just scrolling down on this first page,	
	266:21 it has a date of November 2007. At that point was	
	266:22 the application to have Fentora used for non-cancer	
	266:23 pain pending before the FDA?	
	266:24 A. Yeah, this looks like the application	
	267:1 for that, yeah.	
274:03 - 274:07	**Narayana, Arvind 09-30-2021 (00:00:13)**	NA02.11
	274:3 Q. So, even though patients	
	274:4 were using Fentora and Actiq for chronic pain for	
	274:5 longer than three months, there hadn't been any	
	274:6 controlled trials seeing what would happen to them?	
	274:7 A. Yeah, that's accurate.	
278:03 - 278:03	**Narayana, Arvind 09-30-2021 (00:00:02)**	NA02.12
	278:3 Can we turn to page 12. And, so,	
278:04 - 278:12	**Narayana, Arvind 09-30-2021 (00:00:31)**	NA02.13
	278:4 looking at this, both the text and the table, it's	
	278:5 referring here to an "Analysis of Aberrant Drug-Use	
	278:6 Behaviors In the Clinical Database."	
	278:7 So, someone went through the clinical	
	278:8 database for these non-cancer patients and looked	
	278:9 for these kinds of behaviors?	
	278:10 A. Yeah, I don't know if it was a	
	278:11 pre-specified analysis or if this was done on a	
	278:12 post hoc basis, on a post hoc basis.	
296:11 - 297:20	**Narayana, Arvind 09-30-2021 (00:01:50)**	NA02.14
	296:11 Q. So, the sentence here, it says, "Of the	
	296:12 941 patients who took at least one dose of the	
	296:13 study drug (safety analysis set), 156 (17%) of	
	296:14 patients had at least one aberrant drug-use	
	296:15 behavior identified through review of the	
	296:16 database."	
	296:17 So, the conclusion here is that of	
	296:18 patients who took at least one dose of Fentora in	
	296:19 any of these four studies, 17% of them manifested	

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	296:20 one aberrant drug-use behavior."	
	296:21 Is that correct?	
	296:22 A. Yes.	
	296:23 Q. And what do you think of that 17%	
	296:24 number? Is that a high number or a low number?	
	297:1 A. My understanding, at the time it was a	
	297:2 relatively low number compared to some of the	
	297:3 analyses that were done by other authors.	
	297:4 Q. What do you mean "compared to some of	
	297:5 those other analyses"? Did they show that people	
	297:6 would have a higher rate of aberrant behavior?	
	297:7 A. I recall that -- I recall that it was in	
	297:8 the 40% range. But it was -- these weren't	
	297:9 apples-to-apples comparisons.	
	297:10 Q. Explain what you mean by that.	
	297:11 A. Well, I think, I mean, as mentioned	
	297:12 before, this -- this patient population, patients	
	297:13 with a history of abuse were excluded by my -- by	
	297:14 my recollection and so -- but -- so, that may be	
	297:15 one difference compared to -- compared to some of	
	297:16 the other analyses.	
	297:17 Q. So, in this -- in these studies,	
	297:18 Cephalon excluded patients with a prior history of	
	297:19 substance abuse, didn't they?	
	297:20 A. Yes.	
297:24 - 298:02	**Narayana, Arvind 09-30-2021 (00:00:05)**	NA02.15
	297:24 In the real world, providers might be	
	298:1 prescribing to patients with a history of substance	
	298:2 abuse, right?	
298:05 - 298:06	**Narayana, Arvind 09-30-2021 (00:00:03)**	NA02.16
	298:5 A. Yeah, they may -- they may choose to do	
	298:6 so, yep.	
299:06 - 299:15	**Narayana, Arvind 09-30-2021 (00:00:28)**	NA02.17
	299:6 Q. And you're saying that some of these	
	299:7 observational studies in the real world found that	
	299:8 patients had a higher rate of aberrant behavior,	
	299:9 like 40%, because they had a different patient	
	299:10 base, right?	
	299:11 A. Yeah, that's accurate.	
	299:12 Q. So, in the real world, providers who are	

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	299:13 prescribing to patients might see 41 -- 40% of 299:14 those patients having some sort of aberrant 299:15 behavior over the long-term?	
299:18 - 300:01	**Narayana, Arvind 09-30-2021 (00:00:26)** 299:18 A. It's definitely possible. I think -- I 299:19 think comparing this study, which -- which had a 299:20 different meeting exposure compared to the other 299:21 ones, are definitely challenging. 299:22 But I do think that the fact that these 299:23 Fentora studies excluded patients with a history of 299:24 abuse I think is important in terms of how you 300:1 interpret the results.	NA02.18
300:02 - 300:06	**Narayana, Arvind 09-30-2021 (00:00:12)** 300:2 BY MR. WARD: 300:3 Q. All right. And -- and what studies did 300:4 Cephalon or Teva run on Fentora patients with any 300:5 sort of history of abuse? 300:6 A. I don't recall any.	NA02.19
301:03 - 301:08	**Narayana, Arvind 09-30-2021 (00:00:19)** 301:3 Q. So, patients who had a prior history of 301:4 substance abuse who were being prescribed Fentora 301:5 in the real world, clinicians and patients were 301:6 essentially part of an experiment because there 301:7 hadn't been any prior clinical trials on this 301:8 patient group, right?	NA02.20
301:11 - 302:01	**Narayana, Arvind 09-30-2021 (00:01:00)** 301:11 A. I think that, yeah, there weren't -- 301:12 there were no studies, but I think -- and I also 301:13 co-authored a paper with a few external thought 301:14 leaders, and I think what was communicated in that 301:15 paper is that serious consideration should be -- 301:16 should be given for using a drug like Actiq or 301:17 Fentora in a patient with a history of abuse. 301:18 There is -- there is data to suggest 301:19 from other investigators that the faster the rise 301:20 in plasma levels is more amenable to -- to -- is 301:21 preferred by abusers. And so -- so, I think 301:22 that -- I think we tried to communicate that those 301:23 will probably not be the best patients to use -- to 301:24 use Fentora, but in the end it's the physician's	NA02.21

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	302:1 decision.	
302:03 - 302:17	**Narayana, Arvind 09-30-2021 (00:00:43)** 302:3 Q. Let me understand that. So, you 302:4 published an article with some other thought 302:5 leaders about whether Fentora should be used with 302:6 patients with a prior history of substance abuse. 302:7 Is that correct? 302:8 A. That wasn't -- the title of the article 302:9 was -- it was called "Appropriate" -- I think it 302:10 was "Appropriate Patient Selection, Appropriate 302:11 Use." 302:12 And one of the things I think we 302:13 stressed in that article was that -- that if a 302:14 patient is -- is started on Fentora who has a 302:15 history of abuse, that they should undergo very 302:16 close -- very close monitoring. But that would -- 302:17 that would apply to other opioids also.	NA02.22
304:19 - 305:04	**Narayana, Arvind 09-30-2021 (00:00:28)** 304:19 Q. What about this data here about the 17% 304:20 of patients with aberrant drug-use behavior. Was 304:21 that something that was always disclosed? 304:22 A. Well, I mean our indication was for 304:23 cancer-related breakthrough pain. So, if we did 304:24 get the broad indication, which we didn't, then 305:1 this information would have been part of -- part of 305:2 the information either in the label or in our 305:3 promotional materials. But as you know, we never 305:4 got the expanded indication.	NA02.23
305:05 - 305:07	**Narayana, Arvind 09-30-2021 (00:00:05)** 305:5 Q. So, the answer is no, this information 305:6 wasn't disclosed? 305:7 A. Well, it was --	NA02.24
305:10 - 305:14	**Narayana, Arvind 09-30-2021 (00:00:14)** 305:10 A. It was disclosed in publications, I know 305:11 that. And it -- it wouldn't have -- it would have 305:12 been -- some people would have viewed it as 305:13 off-label promotion to include it within 305:14 promotional materials.	NA02.25
305:16 - 305:21	**Narayana, Arvind 09-30-2021 (00:00:16)** 305:16 Q. So, you had -- you had data from this	NA02.26

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	305:17 group of non-cancer patients showing that 17% of 305:18 the patients had aberrant drug-use behavior even 305:19 though they had no prior history of substance 305:20 abuse, right? 305:21 A. Yep.	
307:19 - 308:15	**Narayana, Arvind 09-30-2021 (00:01:07)** 307:19 All right. So, this is a review by the 307:20 FDA's Center for Drug Evaluation and Research, 307:21 Controlled Substance Staff. 307:22 And going down to the "Summary" it says, 307:23 "Cephalon has filed this 505(b)(2) supplemental New 307:24 Drug Application." 308:1 Have you ever reviewed this document 308:2 before? 308:3 A. Parts of it I'm pretty sure I looked at. 308:4 Q. Let me read the first sentence there. 308:5 It says, "This review provides recommendations to 308:6 the Division of Anesthesia, Analgesia and 308:7 Rheumatology Products regarding the abuse and 308:8 diversion potential of Fentora." Right? 308:9 A. I'm still not clear on if this was -- 308:10 let's see. Oh, I think -- I think given that it 308:11 was a controlled substance, I think the -- there 308:12 is -- yeah, it looks like there is -- the 308:13 Controlled Substance Staff did their own evaluation 308:14 and provided their recommendation to the division 308:15 that was responsible for evaluating the application.	NA02.27
316:03 - 316:05	**Narayana, Arvind 09-30-2021 (00:00:07)** 316:3 Q. Let's go to the next -- the 316:4 paragraph under "Conclusions" that say, "We are 316:5 particularly concerned."	NA02.28
316:06 - 317:06	**Narayana, Arvind 09-30-2021 (00:01:08)** 316:6 All right. So, the first sentence 316:7 there, "We are particularly concerned about the 316:8 training provided to the clinicians running these 316:9 trials as to their recognition of behavior deemed 316:10 'aberrant' and the policies and procedures for 316:11 capturing and coding such behavior, including the 316:12 definitions of addiction, abuse, and diversion 316:13 employed in these studies."	NA02.29

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	316:14 It goes on two sentences later to say, 316:15 "Because this information is not available or 316:16 perhaps was not gathered, the rates of abuse, 316:17 diversion, and aberrant behavior, in general, are 316:18 likely underreported for these clinical trials." 316:19 This is what you were talking about 316:20 earlier with regards to sort of a post hoc analysis 316:21 versus having something planned ahead. Is that 316:22 correct? 316:23 A. I think that's what they're saying, yes. 316:24 Q. They're saying had Cephalon provided 317:1 proper training to clinicians about how to identify 317:2 aberrant behavior and capture and code it, there 317:3 would have been better data on abuse, addiction, 317:4 diversion and aberrant behavior. Is that correct? 317:5 A. Yeah, that's -- that's what they're 317:6 saying.	
318:15 - 319:05	**Narayana, Arvind 09-30-2021 (00:00:53)** 318:15 Q. Let's talk about the FDA's conclusions. 318:16 Conclusion, going down on this page to 318:17 the paragraph with the bullet points under "Based 318:18 on the information available to date," the first 318:19 bullet point says, "Based on the information 318:20 available to date, CSS finds that," bullet point 1, 318:21 "The risks of unintentional potentially fatal 318:22 overdose, as well as misuse or abuse of fentanyl, 318:23 and of Fentora in particular, are extremely high, 318:24 even when compared to risks posed by other 319:1 transmucosal fentanyl products." 319:2 So, the FDA said here that the risks of 319:3 misuse, abuse and overdose of Fentora are extremely 319:4 high. Is that correct? 319:5 A. That's what they're saying.	NA02.30
319:21 - 320:14	**Narayana, Arvind 09-30-2021 (00:00:53)** 319:21 Q. Next bullet point says, "Events observed 319:22 in clinical trials illustrate the significant risks 319:23 of overdose, misuse, abuse, and diversion from 319:24 Fentora. Detection of aberrant drug-use behavior 320:1 in the controlled setting of a clinical trial is 320:2 very unusual and raises concern for the safe use of	NA02.31

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	320:3 this drug in the general outpatient setting. It is 320:4 particularly noteworthy in that 'high risk 320:5 patients' - those with a prior history of drug or 320:6 alcohol abuse or those with a positive drug test - 320:7 were excluded from participation in the clinical 320:8 trials." 320:9 So, the FDA is saying a number of things 320:10 here. First, the FDA says there are significant 320:11 risks of overdose, misuse, abuse and diversion from 320:12 Fentora, right? 320:13 A. Yes, that's what they're -- that's what 320:14 they say.	
321:02 - 321:23	**Narayana, Arvind 09-30-2021 (00:01:12)** 321:2 Q. All right. The last passage I was 321:3 reading on the bullet point 2 on this page from the 321:4 FDA, there is a sentence that said, "Detection of 321:5 aberrant drug-use behavior in the controlled 321:6 setting of a clinical trial is very unusual and 321:7 raises concerns for the safe use of the drug in the 321:8 general outpatient setting." 321:9 Do you agree, Dr. Narayana, there is a 321:10 difference between the controlled setting of a 321:11 clinical trial and general outpatient use? 321:12 A. Yeah. Yeah, I think once you move from 321:13 the controlled setting to a typical outpatient 321:14 setting, there is -- there is different issues. 321:15 And so, yeah, something -- something 321:16 that -- to think about and -- but I would say that 321:17 the -- the inclusion/exclusion criteria that we had 321:18 in our studies were, I think we had some 321:19 investigators actually say that that's -- that's a 321:20 good way of abusing -- using the drugs or opioids 321:21 in general in -- in the real world. 321:22 So, but I think, yeah, I think all 321:23 their -- all their points are valid.	NA02.32
415:15 - 415:22	**Narayana, Arvind 09-30-2021 (00:00:30)** 415:15 So, Exhibit 2, we looked at the FDA's 415:16 Controlled Substances Staff review of the data on 415:17 aberrant drug behavior. Right? 415:18 A. Yes.	NA02.33

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	415:19 Q. In that document the FDA writes that 415:20 risks of overdose, misuse and abuse were extremely 415:21 high for Fentora when used in chronic non-cancer 415:22 pain patients, right?	
416:01 - 416:11	**Narayana, Arvind 09-30-2021 (00:00:36)** 416:1 A. No, I think -- I think they said the 416:2 potential risk. I don't think -- I think they 416:3 were -- they were extrapolating into what they 416:4 thought the use in the real world would look like. 416:5 And so I think they were talking about their 416:6 understanding of the risk is -- was high. 416:7 BY MR. WARD: 416:8 Q. All right. So, in April 2008 the FDA is 416:9 telling Cephalon and you as the medical director 416:10 that Fentora has high risks of abuse and misuse, 416:11 right?	NA02.34
416:12 - 416:17	**Narayana, Arvind 09-30-2021 (00:00:19)** 416:12 A. Yeah, yeah, I think that's accurate. 416:13 Q. And that that's a significant risk of 416:14 Fentora to patients who are using Fentora 416:15 chronically, right? 416:16 A. And that was -- that was on the 416:17 non-cancer data.	NA02.35

Plaintiff Affirmatives = 00:16:14
Defense Counters = 00:01:01
Plaintiff Response Designations = 00:00:16
Total Time = 00:17:31